REMARKS

Claims 1, 2, 7, 36-39, 45-49, and 56-64 are pending and stand rejected. Claims 1, 7, 30-36, 38-44, 47, and 49-55 have been amended; and claims 65-67 have been added. Support for these amendments and new claims can be found in the specification at, for example, page 2, lines 1-8; page 9, lines 11-12; page 9, line 19 to page 10, line 2; page 12, line 21 to page 13, line 18; and Figure 4. No new matter has been added. In addition, Applicant has amended the specification per CFR 1.57(f) to insert material incorporated by reference into the specification. This material was previously incorporated by reference in Applicant's specification at page 2, lines 1-8. The material incorporated into the specification can be found in U.S. Patent No. 6,632,429 at, for example, col. 1, lines 13-24; col. 1, lines 31-39; col. 2, lines 50-55; col. 4, line 66 to col. 5, line 6; col. 6, lines 33-48; col. 9, lines 57-59; col. 10, lines 31-34; col. 10, lines 51-53; and col. 10, lines 58-60. Accordingly, no new matter has been added.

In light of the above amendments and the following remarks, Applicant respectfully requests reconsideration and allowance of the pending claims.

Objection to the specification

The Examiner objected to the specification under 37 CFR 1.75(d) and MPRP § 608.01(o) as allegedly failing to provide proper antecedent basis for the claimed subject matter in claims 56-64. The Examiner requested that Applicant amend the present application to provide antecedent basis for the limitations of claims 56-61. Applicant has herein amended the specification to address the Examiner's concerns. This material was previously incorporated by reference in Applicant's specification at page 2, lines 1-8. The material incorporated into the specification can be found in U.S. Patent No. 6,632,429 at, for example, col. 1, lines 13-24; col. 1, lines 31-39; col. 2, lines 50-55; col. 4, line 66 to col. 5, line 6; col. 6, lines 33-48; col. 9, lines 57-59; col. 10, lines 31-34; col. 10, lines 51-53; and col. 10, lines 58-60. No new matter has been added.

In addition, the Examiner objected to the specification with respect to claims 62-64 stating that Applicant's specification does not specifically teach a method incorporating both the use of conventional tests and the claimed method of diagnosis.

Applicant's respectfully disagree. To comply with the written description requirement, the specification "need not describe the claimed subject matter in exactly the same terms as used in the claims; it must simply indicate to persons skilled in the art that as of the [filing] date the applicant had invented what is now claimed." *Eiselstein v. Frank*, 52 F.3d 1035, 1038 (Fed.Cir.1995) (citing *Vas-Cath v. Mahurkar*, 935 F.2d 1555, 1562, and *In re Wertheim*, 541 F.2d 257, 265 (CCPA 1976)). In fact, after indicating that there is no *in haec verba* requirement, the MPEP states that newly added claim limitations need to be supported in the specification through express, implicit, or inherent disclosure. MPEP § 2163. "The failure of the specification to specifically mention a limitation that later appears in the claims is not a fatal one when one skilled in the art would recognize upon reading the specification that the new language reflects what the specification shows has been invented." *All Dental Prodx, LLC v. Advantage Dental Products, Inc.*, 309 F.3d 774 (Fed. Cir. 2002) (citing *Eiselstein* at 1039), see also, *In re Wright*, 866 F.2d 422 (Fed. Cir. 1989) (reversing the Examiner's new matter rejection based on the phrase "not permanently fixed").

Given Applicant's specification, including the material incorporated by reference from U.S. Patent Nos. 6,534,063 and 6,632,429, one of ordinary skill in the art would be aware of symptoms associated with Autism, for example, multiple distortions in the development of basic psychological functions that are involved in the development of social skills and language, such as attention, perception reality testing and motor movement. In addition, many children diagnosed with Autism suffer from primary diffuse gastrointestinal problems such as protracted diarrhea and constipation. See, for example, Applicant's amended specification and U.S. Patent No. 6,632,429 at col. 1, lines 31-39. Furthermore, one of skill would recognize that noting one or more symptoms of autism is frequently an aspect of diagnosing and monitoring the treatment Autism, for example, through the use of the CARS or ADOS tests. See, for example, Applicant's amended specification and U.S. Patent No. 6,632,429 at col. 6, lines 33-48.

Moreover, a person of ordinary skill in the art would have recognized that knowledge of a person's symptoms of autism would provide additional diagnostic information, and that the combination of symptomatic information and measurements from Applicant's stool immunoassay would yield improved diagnostic accuracy. As described in Applicant's specification, biomarkers of gastrointestinal dysfunction may aid in the diagnosis of PDD's such as autism, ADD, and ADHD. See, for example, page 2, lines 9-14. Thus, the limitations directed toward individuals exhibiting one or more symptoms of autism are supported by the specification.

In light of the above, Applicant respectfully requests withdrawal of the objection to the specification.

Rejection Under 35 U.S.C. § 112, Second Paragraph

The Examiner rejected claims 1, 2, 7, 36-38, 45-49, and 56-64 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner objected to the phrase "identifying the presence of one or more different pathogens in the stool sample as a biomarker that indicates that the individual has Autism." Office Action at page 4.

Applicant respectfully asserts that the claims as unamended were clear and definite, but, in order to further prosecution, has nevertheless amended independent claims 1, 36, and 47 to recite, for example, "determining that the individual has Autism based on the presence of the antigens associated with the two or more different pathogens in the stool sample." Applicant respectfully asserts that this amended language particularly points out and distinctly claims that which Applicant regards as the invention. Accordingly, Applicant requests withdrawal of the rejections.

Rejections under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 1, 2, 7, 36-38, 45-49, and 56-64 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement. Specifically, the Examiner alleged that, while

being enabling for diagnosing Autism, Applicants have not provided sufficient evidence to demonstrate a clear correlation between the presence of any one of the indicated pathogens and Autism.

Applicants respectfully disagree. The test of enablement is whether the specification teaches one skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993). Importantly, "a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must* be taken as in compliance with the enabling requirement of the first paragraph *unless* there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." *In re Marzocchi*, 439 F.2d 220, 222-223 (CCPA 1971) (emphasis in the original).

The claims as amended are fully enabled, particularly in light of Applicant's examples of measuring antigens associated with specific pathogens in stool samples from autistic subjects. As described in pages 12-13 and Figure 4, at least two of the claimed pathogens were detected in the stool samples of individuals diagnosed as having Autism. A person of ordinary skill in the art would have recognized that Applicant has identified a correlation between a diagnosis of Autism and the presence of two or more of the pathogens recited in the present claims. On the basis of this correlation, the skilled artisan would have recognized that Autism could be diagnosed based on the presence of antigens associated with two or more of these pathogens. See, for example, page 13, lines 6-18. The Examiner bears the burden of "providing sufficient reasons for doubting any assertions in the specification as to the scope of enablement." *In re Wright*, 999 F.2d at 1561. The Examiner has not met this burden in the present case as the Examiner has not provided sufficient reasons for doubting the assertions in Applicant's specification as to the existence of a correlation between the presence of two or more of the particular pathogens and a diagnosis of Autism.

As stated in MPEP § 2164.06, the test for enablement is "not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the

specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988) (citing *In re Angstadt*, 537 F.2d 489, 502-04 (CCPA 1976). As described above, the specification of the present application provides such guidance. The specification identifies the correlation between the presence of two or more pathogens and a diagnosis of Autism, and describes how a stool immunoassay can be performed to detect the presence or absence of antigens associated with the specific list of pathogens. With knowledge of routine biochemical and immunological methods, a person of ordinary skill would understand how such immunoassays could be performed without undue experimentation. Thus, one of skill in the art would know how to make and/or use the full scope of the claims.

With respect to claims 47-49, 58, 61, and 64, the Examiner alleged that the specification does not enable methods for determining if a person is at increased risk of developing Autism based on the presence of antigens associated with the indicated pathogens. While the Examiner asserts that Applicant has failed to meet the enablement standard, the Examiner apparently seeks data that would be obtained only from full-blown clinical trials. Specifically, the Examiner noted that "applicant must show that the correlation between those who test positive for the pathogen, and those who have the claimed disorder is not merely allegorical, but has real potential as a diagnostic tool." Office Action of July 29, 2003 at page 6. The Examiner stated that "applicant did not show that children with the disclosed infection were likely to develop the disorder. In order to do so, the applicant would need to show that a percentage of people with the disclosed infections were more likely to develop the diseases than those not infected." Office Action of July 29, 2003 at page 7. Applicant asserts that such a conclusive determination of clinical, therapeutic, or diagnostic efficacy is not required for patentability. Applicant need not await results of clinical trials to claim methods of diagnosis as presently recited. The courts have consistently held that the Examiner's standard is not the proper level of inquiry when assessing enablement under Title 35. As recently held by the Federal Circuit, "providing proof sufficient to justify conducting *in vivo* procedures on humans, while useful, is not a test of patentability." *PharmaStem Therapeutics, Inc. v. Viacell, Inc*., 2007 WL 1964863 at *20 (Fed. Cir. 2007). The

patent applicant need only produce experimental proof that procedures carried out in other systems may be extrapolated for use in humans. *Id*. *See also In re Brana*, 51 F.3d 1560, 1568 (Fed. Cir. 1995) (holding that applicants need not produce data that could only be obtained from Phase II clinical trials to satisfy § 112, first paragraph); *Cross v. Iizuka*, 753 F.2d 1040, 1051 (Fed. Cir. 1985) (holding that successful *in vitro* testing for a particular pharmacological activity may establish a significant probability that *in vivo* testing would be successful). Indeed, the Examiner's assertion that the present specification's examples, which draw a correlation between a patient diagnosed with Autism and the presence of two or more of the claimed pathogens, could not be used as an indicator for an increased risk for developing the disorder seems to directly contradict the prevailing case law, particularly given the fact that the Examiner has not provided any case law to support such a position. Accordingly, given all of the above, Applicant respectfully asserts that it would not require undue experimentation for one having ordinary skill in the art to practice the claimed invention. Withdrawal of the rejections is respectfully requested.

With respect to claims 62-64, the Examiner alleged that "the mere presence of a single symptom would not appear to be indicative of the presence or development of the disorder." Applicant disagrees with this allegation. The test of enablement considers disclosures in the patent coupled with information known in the art. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367 (Fed.Cir.1986). A person of ordinary skill in the art would have been aware of symptoms associated with Autism, and would have recognize that knowledge of a person's symptoms consistent with a diagnosis of Autism would provide additional diagnostic information, and that the combination of symptom information and measurements from the stool immunoassay would yield improved diagnostic accuracy. For example, the Child Autism Rating Scale (CARS) or Autism Diagnostic Observation Schedule (ADOS) tests for Autism are often used to diagnose Autism based on the presence of various symptoms of Autism and were, in fact, the tests used to diagnose the children in Case 4 of Applicant's specification. Based on this disclosure and the knowledge available in the art, one of ordinary skill would understand that Applicant's diagnostic assay could be combined with additional tests, either before, during or

after administration of the assay, and such understanding would not require undue experimentation. For example, the Applicant's assay could be administered to an individual exhibiting one or more symptoms of Autism as described in the CARS or ADOS tests, such as those children provided in the Applicant's Case 4 (see pages 12-13 of Applicant's specification).

In light of these disclosures, a person having ordinary skill in the art would have understood how to make and use the presently claimed invention without undue experimentation. Accordingly, the present claims are fully enabled and Applicant respectfully requests the withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

The Examiner rejected claims 62-64 under 35 U.S.C. § 112, first paragraph, as allegedly being new matter. According to the Examiner, the subject matter of claims 62-64 is allegedly new matter because there is no clear support in the specification or the claims as originally filed for such claims.

Applicants respectfully disagree. To comply with the written description requirement, the specification "need not describe the claimed subject matter in exactly the same terms as used in the claims; it must simply indicate to persons skilled in the art that as of the [filing] date the applicant had invented what is now claimed." *Eiselstein v. Frank*, 52 F.3d 1035, 1038 (Fed.Cir.1995) (citing *Vas-Cath v. Mahurkar*, 935 F.2d 1555, 1562, and *In re Wertheim*, 541 F.2d 257, 265 (CCPA 1976)). In fact, after indicating that there is no *in haec verba* requirement, the MPEP states that newly added claim limitations need to be supported in the specification through express, implicit, or inherent disclosure. MPEP § 2163. "The failure of the specification to specifically mention a limitation that later appears in the claims is not a fatal one when one skilled in the art would recognize upon reading the specification that the new language reflects what the specification shows has been invented." *All Dental Prodx, LLC v. Advantage Dental Products, Inc.*, 309 F.3d 774 (Fed. Cir. 2002) (citing *Eiselstein* at 1039), see also, *In re Wright*, 866 F.2d 422 (Fed. Cir. 1989) (reversing the Examiner's new matter rejection based on the phrase "not permanently fixed").

As described above, given Applicant's specification, including the material incorporated by reference from U.S. Patent Nos. 6,534,063 and 6,632,429, one of ordinary skill in the art would be aware of symptoms associated with Autism, for example, multiple distortions in the development of basic psychological functions that are involved in the development of social skills and language, such as attention, perception reality testing and motor movement. In addition, many children diagnosed with Autism suffer from primary diffuse gastrointestinal problems such as protracted diarrhea and constipation. See, for example, Applicant's amended specification and U.S. Patent No. 6,632,429 at col. 1, lines 31-39. Furthermore, one of skill would recognize that noting one or more symptoms of autism is frequently an aspect of diagnosing and monitoring the treatment Autism, for example, through the use of the CARS or ADOS tests. See, for example, Applicant's amended specification and U.S. Patent No. 6,632,429 at col. 6, lines 33-48. Moreover, a person of ordinary skill in the art would have recognized that knowledge of a person's symptoms of autism would provide additional diagnostic information, and that the combination of symptomatic information and measurements from Applicant's stool immunoassay would yield improved diagnostic accuracy. For example, the Child Autism Rating Scale (CARS) or Autism Diagnostic Observation Schedule (ADOS) tests for Autism are often used to diagnose Autism based on the presence of various symptoms of Autism and were, in fact, the tests used to diagnose the children in Case 4 of Applicant's specification. As described in Applicant's specification, biomarkers of gastrointestinal dysfunction may aid in the diagnosis of PDD's such as autism, ADD, and ADHD. See, for example, page 2, lines 9-14. Thus, the limitations directed toward individuals exhibiting one or more symptoms of autism are supported by the specification and no new matter has been introduced.

Accordingly, Applicant respectfully asserts that claims 62-64 do not include new matter and respectfully requests the withdrawal of the new matter rejection.

CONCLUSION

Applicant submits that the pending claims are in condition for allowance, which action is requested. The Examiner is invited to telephone the undersigned if such further prosecution or expedite allowance of the present case.

Please apply any charges or credits to deposit account 06-1050, referencing Attorney Docket No. 25324-0021001.

Respectfully submitted,

Date: August 10, 2010

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